Specialty Conference

Tetanus

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DR. NYHAN:* We have many things to show and tell this morning. We shall begin with the case presentation by Dr. Young.

DR. YOUNG:** J. was a 12 year old Mexican boy admitted to Children's Health Center in San Diego with chief complaint of generalized rigidity. The history given was that a week, more or less, before admission the patient had cut both feet while playing on an old mattress. Three days before admission progressive generalized rigidity of the jaw, extremities and trunk developed.

Past history indicated that the patient probably never had had DPT immunization. On physical examination he appeared to have no respiratory distress. He had facial trismus and generalized rigidity of the jaw. The extremities and trunk were also rigid, and he assumed an opisthotonic posture. Careful examination of the skin revealed no lacerations or punctures, although there were many minor abrasions over the lower extremities and the chest.

Immediately a dose of 4,000 units of Hyper-Tet® (tetanus immune gobulin, human) was injected intramuscularly and diazepan (Valium®) was administered intravenously until the spasms completely cleared. Treatment with penicillin, one million units every three hours, was begun at the same time. Also given at the beginning of treatment was 60 mg of phenobarbital, and this was repeated every eight hours.

The acute course lasted approximately one week. During this time the total amount of Valium per day peaked at 30 mg, given in 5 mg doses. Toward the second hospital week Valium by mouth controlled the spasms. By the end of the second week there were no more spasms and the patient was discharged 16 days after admission and approximately three weeks from the onset of disease.

Discussion

Dr. Connor* asked me to discuss some of the problems we had and observations we made, since I was with this patient most of the time he was in hospital. The usual incubation period for tetanus is 5 to 14 days. This child had received the cuts on the feet a week, or possibly

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as little as three days, before the development of symptoms. In general, the sooner the onset of symptoms the more severe is clinical tetanus.

Another perplexing factor was the site of infection. We really did not see any puncture wounds or lacerations on the feet or elsewhere. X-ray studies of both feet were negative for foreign bodies. Feeding the patient posed problems. For the first three days he was sustained by intravenous fluids. During the first two days when we did try to feed him even clear fluids in small amounts, trismus was triggered and laryngospasm ensued. By the fourth day of treatment with Valium, trismus had lessened and the patient was able to take clear fluids. By the end of a week he was eating a regular diet.

Spasms occurred about four times as often during the day as at night. We assume that this is because of the stimulation that occurs during the daytime, when even in an intensive care unit there is more activity and the patient was watching television. At night, from approximately midnight to 7 a.m., he had no spasms and we did not use any Valium. Results with Valium in this patient were impressive. He responded completely to as little as a 5 mg dose. More, at one moment he would be completely rigid, and then in the next, following a dose of the drug, he would become completely relaxed.

As this was the first patient with tetanus I had ever treated, my classification as to severity of the disease is not based on experience. I would consider the following factors in classification: (1) the spasms came only with stimulation; (2) the frequency of spasms was not great—the intervals were longer than ten minutes; (3) the duration of spasms was from 10 to 60 seconds; and (4) there was no impairment of the airway. Using these guidelines I would estimate that the patient fits the moderate category of tetany. Since his discharge the patient has done very well.

DR. NYHAN: Dr. Young, tell us what kind of criteria you used for the titration of this patient. How did you decide when he needed 5 mg of Valium?

DR. YOUNG: We calculated a total dose per day at 5 mg per kg of body weight, and this came out to 150 mg per day for this boy. Then we started with 5 mg initially and repeated it slowly until his rigidity disappeared and he became completely calm. The first time, it took approximately 10 to 15 mg. Thereafter, when he had an attack of tetanic spasms, 5 mg was enough. Then we stayed at the 5 mg dose.

DR. NYHAN: How did you select the 4,000 units dose of Hyper-Tet?

DR. YOUNG: We got that from the Red Book,[1] which recommended anywhere up to 5,000 units.

DR. NYHAN: Thank you very much. The management of this patient has relevance to our rotation of residents to Mexico City. Tetanus is endemic in Mexico, and house officers working there should get experience in its management. I would like to turn this discussion over now to Dr. Connor, who is going to show a film and narrate it.

DR. CONNOR: We have prepared a three-minute movie on this patient to illustrate the condition and its treatment with Valium. He was very hypertonic. His rigidity was demonstrated here with sustained clonus following activation of the Achilles stretch reflex. At that time about eight hours had elapsed since his last dose of Valium. Then he was given 5 mg of Valium intravenously. The injection is painful. The material tends to flocculate upon mixing in a very small volume of intravenous fluid. Since it is painful the patient reacts, as demonstrated, with a spasm, and then, gradually at first, then very quickly, he relaxes. The post-Valium relaxation stage is very dramatically different from the rigidity which immediately preceded it. A desirable part of this type of therapy, especially in a mild case, is that it leaves the patient awake, conscious, and responsive.

DR. NYHAN: I was interested to see that during the examination in the film, following the treatment with Valium, the patient had a demonstrably soft abdomen and at a time when he still had some clonus. It has been my experience with patients with tetanus that one of the earliest signs of the return of tetanus following treatment, or the last sign to disappear as they are being effectively managed, is the tension and rigidity of the abdominal musculature. It is usually a useful sign, but it just didn't happen to be in this case, at least on the first day. We shall now turn the discussion over to Dr. Kerr, who is going to consider the management of tetanus.

DR. KERR:* This was, I thought, a very nice demonstration of how well Valium can control mild to moderate tetanus.[2] At the other end of this

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scale, there is a 71-year-old man upstairs, weighing only about twice as much as this boy does, who received 360 mg of Valium over a period of about 12 hours. At the end of this time he was considerably more rigid than at the beginning and was having more in the way of muscle spasms. So general paralysis with curare was employed. While Valium will control the muscular symptoms in some cases, it will not work in all.

Prognostic Criteria in Tetanus

When tetanus is first diagnosed, the symptoms are often not fully developed, but it has proved prognostically useful to consider the rate of development of the disease. The most commonly employed indices of this rate are the incubation and the onset period.[3] The incubation period is the time between injury and the appearance of the first symptom of tetanus; the onset period is that between the appearance of the first symptom and the first major spasm. Short periods of incubation (less than seven days) and of onset (less than 48 hours) are generally followed by more severe tetanus and vice versa.

The boy we are discussing had an incubation period which may have been as short as five days, though it was difficult to date it exactly because he had several minor injuries from any one of which he may have contracted tetanus. His onset period, however, was at least three days, because on admission he was complaining of trismus and stiffness rather than muscle spasms. From this you would have guessed that the course would be moderate rather than severe.

Classification of Severity

Classification is usually done in retrospect on the basis of the symptoms observed during the course of the disease.[4] A case in which only trismus and rigidity develop is classed as mild. If there is dysphagia as well as muscle hypertonicity and perhaps mild spasms, the classification is moderate. If, in spite of treatment, muscle spasms which interfere with ventilation occur, the disease is severe.

Pathophysiology

Clostridium tetani is a Gram-positive rod which grows and produces its toxins only in regions of low oxygen tension. Wounds which are likely to become the site of clostridial growth include deep punctures in which necrotic tissue is present and wounds enclosing a foreign body. The tetanus toxin that causes muscle spasms (tetanospasmin) reaches the central nervous system by way of the nerves or the bloodstream, and probably by a combination of these routes. In the spinal cord it has been shown to affect the ability of the anterior horn cells to produce inhibitory postsynaptic potentials. Thus, the normal balance of excitation and inhibition in the final common pathway to the muscles is upset, excitation becoming preponderant. A good example of this effect was seen in the present case when the boy was stimulated before he had received Valium. The "mass reflex" seen [in the motion picture] after the knee was tapped represented an uninhibited response to the stimulus; the effects persisted (as clonus) and spread up the cord to involve other muscle groups in the absence of the normal modulating influences.

It is worth stressing that tetanus is not an infectious disease in the ordinary sense. People who are looking after patients with tetanus, provided they don't get cuts on themselves infected from the site of infection on the patient, will not catch the disease. I stress this because I recall one operating room superintendent who refused to allow a tetanus patient into her operating room for tracheostomy on the grounds that he was going to infect all the other patients. I also have been questioned by one or two nurses who were worried about catching the disease from patients.

Treatment

General Measures

To ensure that all clostridia are killed, treatment with either penicillin or tetracycline should be started as soon as tetanus is suspected. The focus of infection should be sought, and, if found, surgical debridement and excision should be carried out to prevent further toxin production. All patients with established tetanus should receive human anti-tetanus immunoglobulin, preferably before wound excision. Published series have cast some doubt on the usefulness of these measures, but, in view of the difficulty in predicting the likely course of the disease from the early symptoms, it is almost impossible to get a true assessment of any moderating effect that may be exerted by these general measures.

Muscular Hypertonicity

The trismus and increased muscle tone in mild cases of tetanus can usually be controlled adequately with Valium given either orally or parenterally. This is probably the agent of choice at present. Mephenesin and chlorpromazine are two other centrally active muscle relaxant and sedative drugs which have been widely and fairly effectively employed in this disease.

Dysphagia

The hypertonicity of the masseters which produces the "locked jaw" of tetanus is often accompanied by increased tone and incoordination of the swallowing mechanism, resulting in dysphagia. This symptom usually appears early in the course of the disease and may be demonstrated as an inability to swallow saliva so that the patient drools or spits it out, or has a tendency to cough or clear the throat after attempting to swallow. Dysphagia may lead to two particularly dangerous situations.

First, swallowed material may be directed into the larynx, which has intact sensation but whose motor innervation may be irritable. Glottic spasm, usually accompanied by a generalized muscle spasm, often results, so that the body's oxygen supply is cut off at a time when the need is greatest. Children, especially, become cyanotic almost instantly, and a dangerous level of hypoxia may be reached very rapidly.

Second, with persistent dysphagia inhalation of oral contents may lead to aspiration pneumonia. Therefore, if dysphagia develops orotracheal intubation should be carried out after the patient has been anesthetized with thiopentone and relaxed with succinylcholine. The muscle relaxation brought about by these drugs makes it possible to open the mouth even though trismus may have been severe. After endotracheal intubation, trachesostomy can be done at a convenient time, preferably under sterile conditions in an operating room and under general anesthesia. Emergency tracheostomy under local anesthesia is to be avoided because of the danger of inducing glottic spasm during manipulation of the trachea.

After tracheostomy, the inspired gas should be well humidified, regular and effective chest physiotherapy should be carried out, and every precaution taken to prevent lung infection. It is my impression that first class respiratory care can more than halve the reported mortality rate of 70 percent in untreated cases.

Muscle Spasms

Muscle spasms in tetanus can be either localized or generalized and of varying severity. Sustained contraction of the muscles is exhausting, painful, and, when the respiratory muscles become involved, dangerous. Centrally acting muscle relaxants such as Valium and chlorpromazine will control the milder spasms, but these drugs seem less effective in controlling spasms than in relieving rigidity. If large doses are employed in an attempt to control severe spasms, there is a risk that over-sedation will lead to hypoventilation between spasms. In this situation, and when muscular spasms themselves interfere with ventilation, the treatment of choice is general paralysis with curare and intermittent positive pressure ventilation. The results have been better when it is used early in the course of the disease than after prolonged attempts with sedative agents.

Once curarization and ventilation have commenced, barbiturates such as pentobarbital may be used to induce mild hypnosis. Some form of sedation is probably desirable, for despite reassurance many patients who are paralyzed but conscious will be frightened. In some of the most severe cases, however, particularly in old people, the patients may become unresponsive and appear comatose for periods of one to three weeks during the critical phase of their illness. They recover consciousness during the recovery phase and appear normal except for amnesia. In these patients sedative agents should be kept to a minimum.

Because of the bitter experience of having adult patients die of pulmonary embolism in the recovery phase after very severe tetanus, it has been our practice over the last seven years to give anticoagulants to any patient who has required curarization and ventilation. We begin this therapy 24 to 48 hours after tracheostomy and continue it until the patient is fully mobile again. Pulmonary embolism is much commoner in patients with tetanus than in paralyzed patients with other conditions treated in a similar manner, and in some series it was the cause of death in 20 percent of the fatal cases.

Nutrition

Patients with mild tetanus may be fed orally but if dysphagia develops, nasogastric feeding is preferable. While inserting a nasogastric tube at another time entails a risk of inducing glottic spasm, we have found that it can be done safely and conveniently while the patient is anesthetized for tracheostomy.

The chief advantages of nasogastric over intravenous feeding are that the considerable caloric and fluid requirements can be satisfied cheaply and effectively over the two to four weeks that patients with moderate or severe tetanus usually remain dysphagic. In addition, since tube feedings normally contain milk, the incidence of peptic ulceration is considerably reduced. This complication has been quite common in some series and almost invariably fatal in severe tetanus. Paralytic ileus has been reported fairly frequently in association with severe tetanus, but it usually responds to intermittent gastric drainage followed by the installation of antacid and anti-cholinesterase agents such as bethanechol.

Sympathetic Overactivity in Tetanus

In our series,[5] the mortality rate among patients with mild or moderate tetanus is well under 10 percent, but in the severe cases it has remained at about 40 percent in spite of adequate

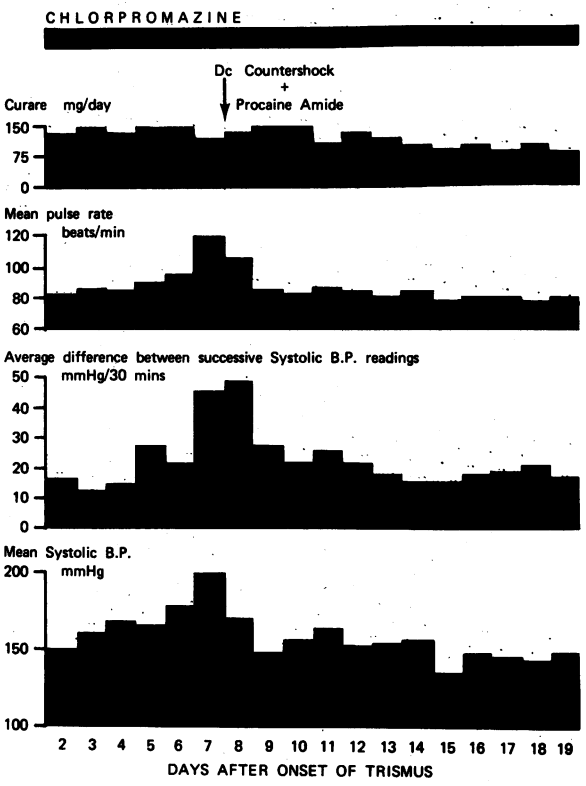

Chart 1.—Changes in 24 hour average systolic blood pressure (BP), variability of blood pressure, mean pulse rate, and curare requirements in a 58-year-old man with severe tetanus. The variability of BP is expressed as the average difference between successive half hourly readings of systolic pressure.

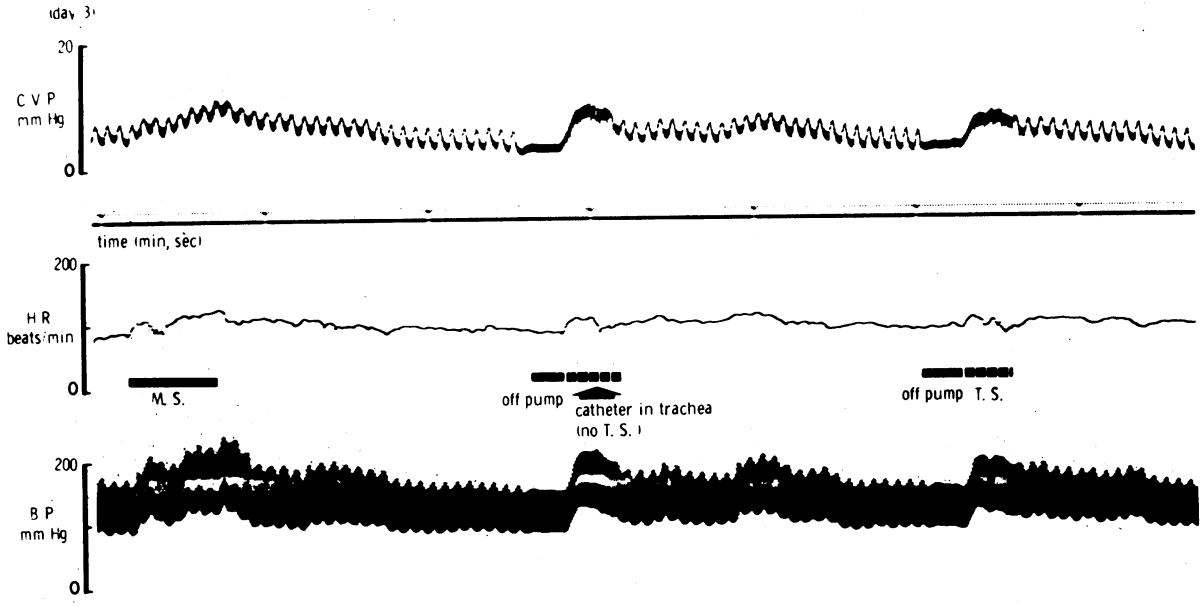

Chart 2.—Variations in central venous pressure (CVP) heart rate (HR), and arterial blood pressure (BP) in a 41-year-old man during oral suction (MS), insertion of catheter into the trachea (no suction), and tracheal suction (TS).

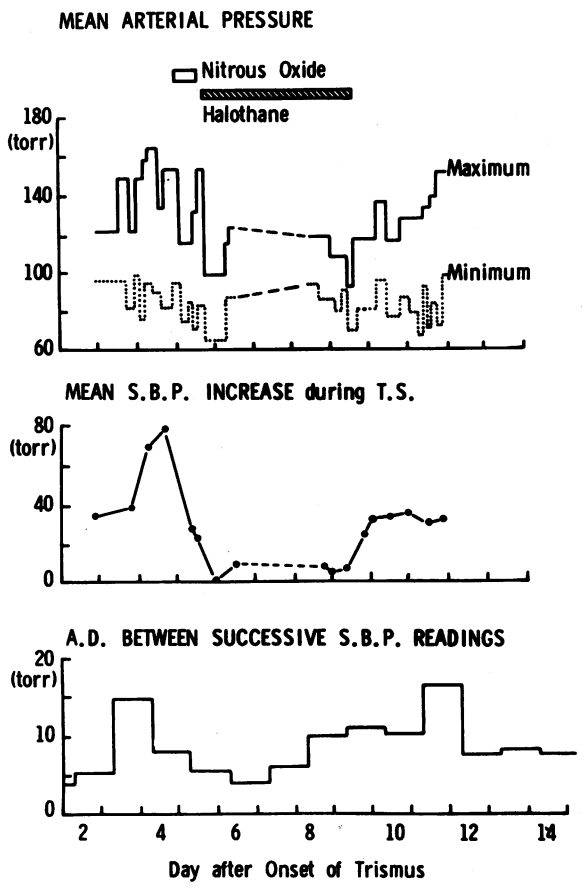

Chart 3.—Assessment of sympathetic nervous activity in a 9-year-old boy with severe tetanus. Changes in mean arterial pressure, mean systolic blood pressure (SPB) increase during tracheal suction (TS), and variability of the systolic blood pressure with time and therapy. Blood pressure variability is expressed as the 24-hour average difference (AD) between successive readings of systolic pressure.

control of the muscular symptoms, prevention of pneumonia, and other measures mentioned above. Postmortem examinations have been unrewarding, but a study of the clinical courses of patients with severe tetanus—both fatal and non-fatal—showed that in many cases there were features suggesting that the sympathetic nervous system was overactive. It is possible that tetanus toxin acts on both the anterior horn cells, causing the classical muscular symptoms, and the lateral horn cells. If inhibition within the sympathetic nervous system were blocked, exaggerated and incoordinated autonomic activity might be predicted.

Among the clinical features shown by patients with severe tetanus were the following:

- A temporary hypertension associated with tachycardia (Chart 1), which occurred even if patients were being treated with doses of sedative agents such as chlorpromazine up to 600 mg a day.

- Increased variability of the blood pressure due in part to spontaneous changes in pressure and in part to exaggerated circulatory responses to stimuli. Among these stimuli was the procedure of aspirating secretions from the trachea (Chart 2). The cardiovascular response to tracheal suction paralleled the degree of cardiovascular instability and increased with increasing variability of the blood pressure, (Chart 3). The response to this stimulus is much more pronounced in patients with tetanus than in other paralyzed patients such as those with myasthenia gravis or acute polyneuritis.

Another autonomic stimulus which has been investigated is Valsalva's maneuver. In this maneuver, the increased intrathoracic pressure impairs transpulmonary blood flow, and the systemic blood pressure falls. The hypotension stimulates the baroreceptors so that sympathetic tone increases to restore the blood pressure. After release of the raised intrathoracic pressure, blood flow through the lungs resumes, and the blood pressure increases. There is normally an "overshoot" in pressure because of residual sympathetic activity, but in patients with tetanus the "overshoot" is exaggerated and prolonged (Chart 4). This is explainable on the basis of an irritable and underinhibited sympathetic nervous system and is the autonomic concomitant of the muscular "mass reflex" that was observed when the boy's knee was tapped.

- Other clinical findings that have contributed to the picture of an overactive and incoordinated sympathetic nervous system include high cardiac output with low arteriovenous oxygen content differences, day-by-day increase in systemic vascular resistance, profuse sweating in normothermic patients, and hyperpyrexia in the absence of infection.

- Metabolic observations have included high carbon dioxide outputs in paralyzed patients, raised plasma catecholamine levels, and increased catecholamine excretion.

Continued sympathetic overactivity is known to have deleterious effects, and an improved prognosis has followed the use of adrenergic

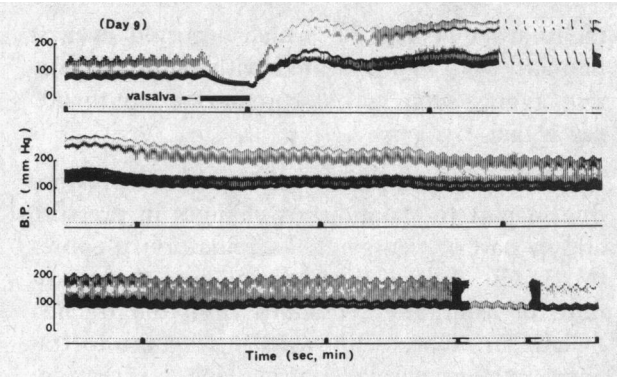

Chart 4.—Arterial blood pressure changes during Valsalva's maneuver in a 74-year-old man on the ninth day after the onset of trismus.

blocking agents in other conditions in which the sympathetic nervous system is overactive (pheochromocytoma and thyrotoxic crisis, for example). These agents have been used on a limited scale in patients with sympathetic overactivity in severe tetanus. The results were encouraging. To permit rational use of these agents and to deepen understanding of the autonomic involvement in this disease, continuous monitoring of cardiovascular variables is essential. The conventional quarter-hourly or half-hourly auscultatory blood pressure reading becomes insufficient in a situation in which the systolic blood pressure may fluctuate irregularly between 50 and 250 mm of mercury within a space of 5 minutes.

The Tetanus Unit

In view of the decreasing incidence of tetanus and of the increasing complexity of the methods used in managing it, in Britain and in France patients with tetanus from a fairly wide area are transported to specially designated tetanus units.[6] These units are usually based on existing respiratory care units and are likely to treat several cases of tetanus each year. Expertise in handling this treacherous disease develops, and results of treatment have improved. The overall case fatality rate from the tetanus units in Britain was 22 percent for the decade up to 1968, and that for one of the largest French units was 33 percent for the period 1961 to 1964. In this country the New Orleans group, which also has a continuing experience with the disease, has reported a similar case fatality rate.

For the United States as a whole[7] the case fatality rate remained at more than 65 percent in both 1965-66 and 1968-69, the contrast suggesting setting up regional tetanus units in this country.

DR. NYHAN: Thank you very much, Dr. Kerr. I'd like now to request some comments from Dr. Connor.

Additional Considerations

DR. CONNOR: Dr. Kerr has given us a very lucid description of the treatment of patients with advanced clinical tetanus. It might be timely to draw a comparison between patients with severe disease and those with mild to moderate disease in relation to control and prevention of repetitive spasms.

In the past almost all the methods used included one or several drugs which, in addition to blocking or lessening spinal cord activity, also depressed cortical activity and activity in the centers of control of other vital functions, particularly respiration. Therefore, the physician was almost always dealing with a patient who was not only relaxed but also made semi-comatose or comatose. As a consequence the dangers of therapy may at times have been greater than those of the disease, since respiratory complications due to the inability to cough, handle secretions or swallow were not uncommon. The highly desirable effect of diazepam (Valium) in controlling spasms and hypertonicity without depression of cortical and other higher centers has made it the drug of choice in the treatment of clinically moderate tetanus. I would like to add that in my experience, as in Dr. Kerr's, if one is unable to attain a state of control of spinal cord activity over a fairly long period after the intravenous administration of Valium, and if increasing doses are required at shorter intervals, then the patient probably cannot be controlled with this drug. High doses, given at frequent intervals, may lead to respiratory depression and hypotension. Inability to achieve control with Valium is indicative of progressive and severe clinical disease. The total dose that one has to go to initially in determining whether or not the patient can be controlled with Valium is about 1 to 2 mg per kilogram of body weight, given in fractional doses. It is usually advisable to start with a fairly small dose intravenously, such as 2 to 5 mg, particularly when the patient has received other medications, especially barbiturates.

TABLE 1.—*Tabulation of Reported Cases of Tetanus in the United States in 1968 and 1969**

Type of Wound	*Cases with a Given Injury*	*Percent of Total Cases*	*Fatal Cases*	*Case-Fatality Ratio*
Puncture	87	29.3	55	63.2
Laceration	84	28.3	48	57.1
Miscellaneous	42	14.1	28	66.7
Abrasion	28	9.4	16	57.1
No Wound	22	7.4	13	59.1
Injection	20	6.7	15	75.0
Crush	10	3.4	5	50.0
Surgical	3	1.0	2	66.7
Dental	1	0.3	0	...
Total	297	100	182	61.3

*Excludes neonates, one person of unknown age, and cases with unknown outcome.

Passive Immunization

Another comment I would like to make bears on the question of passive immunization with hyperimmune tetanus globulin.[8] There are now a number of studies which compare the efficacy of varying amounts of hyperimmune globulin (made in horses or other animals) to no antitoxin at all or to a small dose of antitoxin. Most of these studies support the opinion that antitoxin administered after tetanus has developed is not effective in reducing the morbidity or mortality of the disease. However, an occasional study has shown otherwise, and in my opinion it is wise to continue to use moderate amounts of the human antitoxin in all cases in the dose ranges mentioned by Dr. Young.

Prevention

Now, I would like to consider a few other aspects of tetanus which may be more important than treatment. The first of these is prevention by immunization. Immunization against tetanus is one of the most effective of all public health measures. The detoxified protein exotoxin of Clostrodium tetani is almost always used in combination with a similarly detoxified protein toxin of the diphtheria bacillus, and these, together with a highly concentrated bacillary vaccine of pertussis, are given as injections three or four times during the early months or years of life.

One way to assess the efficacy of such immunizations and boosters is to look at the cases of tetanus occurring during a given period. Table 1 lists reported cases of tetanus occurring in a recent 24-month period in this country.[7] Ninety-six percent of the patients had received no tetanus immunization, by history; 4 percent had received two or more injections, by history. Thus immunity after immunization is at least 95 percent effective. In groups such as the Armed Forces where immunizations are routine and boosters are regularly administered, statistical evaluation indicates an even higher order of protection. The mortality rate in the civilian cases, based upon the 1968-69 surveillance data, is approximately the same in the immunized as in the unimmunized. However, other data, published by Takos from Dade County, Florida, suggested that the mortality rate was significantly decreased in immunized patients in whom the disease developed.

Duration of Protection

Another common question regarding tetanus immunization is the duration of protective antibody levels in properly immunized persons. I think there is no direct answer to that question, since the measurement of antitoxic antibody in serum only allows the conclusion of presence of antitoxic antibody, for what is protective against a minor infection with the tetanus bacillus may not be protective at all against an infection resulting from massive crushing injury, or a long standing, deep puncture wound with persistent anerobiosis. Therefore, it is usually recommended that the periods between re-immunizations be kept short enough to maintain adequate protection from the clinical disease throughout the interval. At present this period is thought to be five to ten years in cases where there are no injuries requiring an immediate booster.

Response to Boosters

Another question relates to the length of "immunologic memory" of the host in respect to primary immunization. In the past there were reports that a rapid secondary (booster) response could be attained several years after a primary series, and then later reports made this ten to fifteen years. Now we know that even after 20 years the booster response occurs just as rapidly as it does in a person who is only five years away from the primary series. With respect to the booster response the antibody which mediates adequate protection is dependably elevated after an interval of approximately five to seven days after the injections. If protection is required be-

fore that time, then one must resort to the use of passive immunization with antitoxin.

The administration of human antitoxin is certainly superior to the old method of using horse serum antitoxin, in two respects. The first is that there is no reaction to the single administration of human globulin antibody, and the second is that the homologous protein in the circulation persists over a much longer period than the heterologous protein in the horse serum. Adequate protection is conferred by the use of 200 to 500 units intramuscularly at the time of injury. In my opinion, in the case of a persistent wound which is complicated by development of non-viable tissue, it would be well to repeat this dose one or more times at ten-day intervals.

Use of Immune Globulin (Human)

DR. HAMBURGER:* I would like to expand on Dr. Connor's comments on the immunotherapy of tetanus. The toxin elaborated by Clostridium tetani has been known to have an extraordinarily high, selective affinity for the cholinergic terminals of nerves. That is why once the toxin has been bound, antitoxin is ineffective. Most of our knowledge of tetanus antitoxin is derived from animal studies, but with the availability of a safe preparation for human use, its *early* use in tetanus is mandatory, and its prophylactic use in wound debridement or in suspected cases is highly recommended.

The present tetanus immune globulin (human) is a solution of gamma globulin prepared from venous blood of humans hyperimmunized with tetanus toxoid. It is 25 times concentrated Cohn Fraction II, containing 165 mg per ml of immunoglobulin, predominantly Immunoglobulin G. Its use carries little of the risk of allergenic sensitization or serum sickness commonly encountered with horse-derived antitoxin. Where the horse serum antitoxin was cleared from the patient's bloodstream and tissues in 8 to 15 days, the TIG (human) has a half-life of 25 days. It persists in adequate concentration for a period long enough to protect adequately while active immunity is being induced. For prophylaxis in an unimmunized person, 250 units (1.0 ml) intramuscularly will provide the adequate protection of a serum level of 0.1 unit per ml for over three weeks. The first immunizing dose of tetanus toxoid (0.5 ml intramuscularly) should be given within that period. For therapy 3,000 to 6,000 units (12 to 24 ml) intramuscularly is recommended. When confronted with a patient with a wound, unless there is documentable evidence of two or more tetanus toxoid injections or of completed immunization against tetanus, the patient should be regarded as not immunized and the TIG (human) as well as a tetanus toxoid booster should be given.

*Robert N. Hamburger, M.D., Professor and Head, Pediatric Immunology and Allergy Division.

Questions and Answers

Question: At what point in therapeutic management do you administer tetanus antitoxin?

DR. CONNOR: It has been shown that when you have a wound infected by Clostridia, there is often a lot of toxin in the tissue around the wound, and it would seem logical to give the immunoglobulin before the wound is debrided, for the debridement process may mobilize toxin. When no wound or locus of infection is found, you should still give antitoxin at the earliest moment.

Question: How often are you unable to find the causative lesion?

DR. CONNOR: In many cases no wound is uncovered by history or by examination. If you look at obvious wounds which are thought to be the source of infection, culture is productive 25 to 35 percent of the time in good laboratories; so it is more common not to find the organism by culture than it is to find it, even in significant injuries.

DR. NYHAN: I have one comment on the question of the wound. Certainly we often do not find a wound in a patient with tetanus. On the other hand, our experience would say that an all-out search should still be made to find it, particularly these days when more children than ever walk around barefoot. I am reminded of the girl we saw with severe tetanus who turned out to have stepped on a chicken bone which lodged between her metatarsals, and the skin healed over it. It has become a reflex with me to make x-ray examination of the feet of children with tetanus.

Question: How often do you see emboli as a complication to therapy? Which risk is greater, emboli or anticoagulants?

DR. KERR: All the pulmonary emboli I have seen have been in older patients. Perhaps children do not get this complication. It is probably more

important to ensure that tetanus patients do not become dehydrated than to anticoagulate them. Apart from one episode of hematuria, we have seen no complications of the anticoagulant therapy as such.

Question: Is there any sign or symptom during the incubation period to warn you that you may be dealing with tetanus?

DR. CONNOR: I have seen delays in diagnosis of as much as 96 hours in patients in whom the initial presenting symptom was dysphagia, diagnosed as sore throat by a physician and treated with antibiotics. I have also seen cases with mild to moderate trismus going on for two to three days diagnosed as phenothiazine reaction or hysteria, then, with progression, diagnosed as tetanus. In the early stages, general hypertonicity and particularly tightness of the abdominal wall muscles anteriorly are helpful in diagnosis. Attempts to demonstrate trismus are also very helpful, for the patient may not know that trismus is present. Spasms induced by stimulation, without loss of consciousness, which are repetitive and spread to skeletal muscles should immediately call attention ot the possibility of tetanus.

Question: Is a patient immune after he has had tetanus?

DR. CONNOR: No, he may not be immune as a result of the infection and the disease. Perhaps the toxin elaborated is not in sufficient amounts to immunize or it is tied up by receptors in the nervous system before it can be recognized by the reticuloendothelial system. Therefore, all patients who recover from tetanus should receive primary or booster immunization.

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THE WAXY SKIN IN SYSTEMIC SCLEROSIS

"The cardinal manifestation of progressive systemic sclerosis is the hard waxy skin. It's true that you sometimes have patients with progressive systemic sclerosis who do *not* have the hard skin, but by and large this is the way you make the diagnosis. The change in skin texture begins at the periphery of the body and progresses centrally. There is great variability in the speed with which it progresses. In some patients it just seems to gallop up the arms into the face. In others sometimes spoken of as having acrosclerosis—I probably should think of them as a separate group—it will remain below the wrist for 15 years and in fact, never advance beyond that."

—JOHN L. DECKER, M.D., Bethesda
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